3. Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA*. 1989;262:2395–401.
4. Blair SN, Kampert JB, Kohl HW, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA*. 1996;276:205–10.
5. Bray GA. Fat distribution and body weight. *Obes Res*. 1993;1: 203–5.
6. Cooper KH. A means of assessing maximal oxygen intake; correlation between field and treadmill testing. *JAMA*. 1968;203:201–4.
7. Duncan JJ, Gordon NF, Scott CB. Women walking for health and fitness; how much is enough? *JAMA*. 1991;266(22):3295–9.
8. Farrell SW, Braun L, Barlow CE, Cheng YJ, Blair SN. The relation of body mass index, cardiorespiratory fitness, and all-cause mortality in women. *Obes Res*. 2002;10:417–23.
9. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Intern Med*. 2008;160:2117–28.
10. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendations for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1423–34.
11. Hu FB, Willett WC, Li T, et al. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med*. 2004;351:2694–703.
12. Gulati M, Pandey DK, Arnsdorf MF, et al. Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation*. 2003;108:1554–59.
13. Jackson AS, Pollock ML. Practical assessment of body composition. *Phys Sportsmed*. 1985;13:1376–90.
14. Katzmarzyk PT, Craig CL, Bouchard C. Adiposity, adipose tissue distribution, and mortality rates in the Canada Fitness Survey follow-up study. *Int J Obesity*. 2002;26:1054–59.
15. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. *JAMA*. 2009;301(19):2024–35.
16. Koster A, Leitzmann MF, Schatzkin A, et al. Waist circumference and mortality. *Am J Epidemiol*. 2008;167:1465–75.
17. Koster A, Harris TB, Moore SC, et al. Joint associations of adiposity and physical activity with mortality. *Am J Epidemiol*. 2009; 169(11):1344–51.
18. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow-up of participants in the population study of women in Gothenburg, Sweden. *Br Med J*. 1984;289:1527–61.
19. Lee CD, Jackson AS, Blair SN. Cardiorespiratory fitness, body composition and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69:373–80.
20. Lyerly GW, Sui X, Lavie CF, Church TS, Hand GA, Blair SN. The association between cardiorespiratory fitness and risk of all-cause mortality among women with impaired fasting glucose or undiagnosed diabetes mellitus. *Mayo Clin Proc*. 2009;84(9):780–6.
21. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. *N Engl J Med*. 1995;333:677–85.
22. Mora S, Redberg RF, Cui Y, et al. Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the Lipid Research Clinics Prevalence Study. *JAMA*. 2003;290(12):1600–7.
23. Ogden CL, Carroll MD, McDowell MA, Flegal KM. Obesity among adults in the United States—no statistically significant change since 2003–2004. *NCHS Data Brief*. 2007;1:1–8.
24. Pollock ML, Foster C, Schmidt D. Comparative analysis of physiologic responses to three different maximal graded exercise test protocols in healthy women. *Am Heart J*. 1982;103:363–73.
25. Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. *JAMA*. 1998;280:1843–8.
26. Simpson JA, MacInnis RJ, Peeters A, et al. A comparison of adiposity measures as predictors of all-cause mortality: the Melbourne collaborative cohort study. *Obesity*. 2007;15(4):994–1003.
27. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. *Am J Epidemiol*. 1984;119(5):837–9.
28. Tanko LB, Bagger YZ, Qin G, et al. Enlarged waist combined with elevated triglycerides is a strong predictor of accelerated atherogenesis and related cardiovascular mortality in postmenopausal women. *Circulation*. 2005;111:1883–90.
29. Wang C, Haskell WL, Farrell SW, et al. Cardiorespiratory fitness levels among US adults 20 to 49 years of age: findings from the 1999–2004 National Health and Nutrition Examination Survey. *Am J Epidemiol*. 2010 Feb 15;171(4):426–35.
30. Weinstein AR, Sesso HD, Lee IM, et al. The joint effects of physical activity and body mass index on coronary heart disease risk in women. *Arch Intern Med*. 2008;168(8):884–90.
31. Westerterp KR. Assessment of physical activity; a critical appraisal. *Eur J Appl Physiol*. 2009;105:823–8.
32. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women: risk within the "normal" weight range. *JAMA*. 1995;273:461–5.

論文名	Cardiorespiratory fitness, adiposity, and all-cause mortality in women
著 者	Farrell SW, Fitzgerald SJ, McAuley PA, Barlow CE
雑誌名	Med. Sci. Sports Exerc.
巻・号・頁	42(11) 2006-2012
発行年	2010
PubMedリンク	http://www.ncbi.nlm.nih.gov/pubmed/20351588

対象の内訳

	ヒト	動物	地 域	欧米	研究の種類	縦断研究
対象	一般健常者	空白		( )		コホート研究
性別	女性	( )		( )		( )
年齢	生存者44.8歳(± [redacted]		4歳(±10.9)	( )		前向き研究
対象数	10000以上			( )		( )

調査の方法	実測	( )				

アウトカム

予 防	なし	なし	なし	なし	死亡	( )
維持・改善	なし	なし	なし	なし	( )	( )

図 表

TABLE 4a. Risk of mortality according to CRF and body composition groups in 11,335 women (CCLS, 1979–2006).

	HR[a] (95% CI)	HR[b] (95% CI)	HR[c] (95% CI)	HR[d] (95% CI)	HR[e] (95% CI)
CRF					
Low fit	1.0	1.0	1.0	1.0	1.0
Moderate fit	0.60 (0.44–0.82)	0.61 (0.44–0.84)	0.61 (0.45–0.84)	0.60 (0.44–0.83)	0.61 (0.44–0.83)
High fit	0.54 (0.40–0.75)	0.57 (0.41–0.79)	0.57 (0.41–0.80)	0.55 (0.40–0.77)	0.56 (0.40–0.79)

[a] Adjusted for age, examination year, current smoking status, and health status.
[b] Model 1 + BMI.
[c] Model 1 + W/HT.
[d] Model 1 + WC.
[e] Model 1 + %BF.

図表掲載箇所

P2009, Table4a

概 要(800字まで)

本研究は、Cooper Center Longitudinal Study(CCLS)に参加した11,335名の女性を対象に1970年から2005年まで追跡調査し、全身持久力や肥満と総死亡の関連について検討したものである。BMIにより対象者を標準体重(BMI=18.5-24.9kg・m-2)と過体重/肥満(BMI>=25.0kg・m-2)に、腹囲により標準(WC<88cm)と高い(WC>=88cm)に、体脂肪率により標準(%BF<30%)と高い(%BF>=30%)に、腹囲・身長比により標準(W/HT<0.5)と高い(W/HT>=0.5)にそれぞれ肥満度を分類した。また、漸増負荷試験による最大酸素摂取量(全身持久力)の測定により、年齢で調節後三分位(低、中、高)に分類した。全身持久力:低のグループと比較すると、全身持久力:中で総死亡リスクが0.60(95%信頼区間:0.44-0.82)、全身持久力:高で0.54(0.40-0.75)と有意にリスクが減少した。さらに、全身持久力上位80%をFitとし下位20%をUnfitと分類すると、Unfitに分類される女性は、標準体重かつFitの女性と比較すると、すべてのBMIの分類において総死亡のリスクが有意に増加した。また、体脂肪率、腹囲、腹囲・身長比が高いグループでもFit(上位80%)のグループは、Fitかつ標準体重のグループと比較しても総死亡リスクがそれぞれ1.0、0.9、1.2と有意な差は見られなかった。

結 論(200字まで)

全身持久力の低い女性は肥満度に関わらず総死亡リスクが有意に上昇するが、全身持久力の高い女性は肥満傾向であっても、総死亡リスクの上昇はみられないことが明らかになった。

エキスパートによるコメント(200字まで)

身体活動基準の策定に用いられた研究の1つである。全身持久力が死亡や様々な疾患のリスクと関連していることは、これまでの研究により報告されていたが、BMIとの相互作用を見た場合、全身持久力が高い人は、BMIが肥満と分類されいている集団でも、リスクを下げることが示されたことは非常に意義深い。

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Exercise Capacity and the Risk of Death in Women : The St James Women Take Heart Project

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Circulation 2003, 108:1554-1559: originally published online September 15, 2003
doi: 10.1161/01.CIR.0000091080.57509.E9
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

Clinical Investigation and Reports

Exercise Capacity and the Risk of Death in Women

The St James Women Take Heart Project

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Background—Cardiovascular disease is the leading cause of death among women and accounts for more than half of their deaths. Women have been underrepresented in most studies of cardiovascular disease. Reduced physical fitness has been shown to increase the risk of death in men. Exercise capacity measured by exercise stress test is an objective measure of physical fitness. The hypothesis that reduced exercise capacity is associated with an increased risk of death was investigated in a cohort of 5721 asymptomatic women who underwent baseline examinations in 1992.

Methods and Results—Information collected at baseline included medical and family history, demographic characteristics, physical examination, and symptom-limited stress ECG, using the Bruce protocol. Exercise capacity was measured in metabolic equivalents (MET). Nonfasting blood was analyzed at baseline. A National Death Index search was performed to identify all-cause death and date of death up to the end of 2000. The mean age of participants at baseline was 52±11 years. Framingham Risk Score–adjusted hazards ratios (with 95% CI) of death associated with MET levels of <5, 5 to 8, and >8 were 3.1 (2.0 to 4.7), 1.9 (1.3 to 2.9), and 1.00, respectively. The Framingham Risk Score–adjusted mortality risk decreased by 17% for every 1-MET increase.

Conclusions—This is the largest cohort of asymptomatic women studied in this context over the longest period of follow-up. This study confirms that exercise capacity is an independent predictor of death in asymptomatic women, greater than what has been previously established among men. The implications for clinical practice and health care policy are far reaching. (***Circulation*. 2003;108:1554-1559.**)

Key Words: exercise ■ epidemiology ■ mortality ■ women

Coronary artery disease (CAD) is the leading cause of death in both men and women in the United States. Women differ from men in their clinical presentation of CAD, their performance on diagnostic tests, and their prevalence of CAD. However, most of the available data on the noninvasive diagnosis of CAD are based on studies in men. Because the pretest likelihood of CAD, referral patterns and diagnostic ability of available tests probably differ for women, the clinical evaluation of women is difficult.[1,2]

See p 1534

The standard exercise ECG is the most commonly used and the least costly noninvasive test to identify CAD. The value of the exercise ECG comes from the wealth of information that can be extracted from the test to provide important prognostic and diagnostic information.[3] Epidemiologic studies have noted that exercise capacity is an independent predictor of cardiovascular events and all-cause death in men.[4–11] Most studies examining the predictive value of exercise capacity have included almost exclusively male subjects[4,5,7,8,10,11] or were retrospective studies.[12] Also, most studies examining exercise capacity included only subjects with established CAD or cardiac symptoms.[5,6,11–14] A prior study that included asymptomatic women showed an association between exercise capacity and death, but their extensive exclusion criteria limit the generalizability of their findings.[15] Previous research has not evaluated all potential prognostic indicators from stress tests in asymptomatic women; therefore, the American College of Cardiology (ACC)/American Heart Association (AHA) Committee on Exercise Testing has identified this as an area in need of further study.[3]

In this study, we assess the prognostic value of exercise capacity in asymptomatic women. The aim of this paper is to determine whether exercise capacity is an independent predictor for all-cause death in asymptomatic women.

Received May 6, 2003; revision received July 15, 2003; accepted July 15, 2003.

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Circulation is available at http://www.circulationaha.org

DOI: 10.1161/01.CIR.0000091080.57509.E9

Methods

This study was approved by St James Hospital and Rush-Presbyterian-St Luke's Medical Center's Institutional Review Board.

Participants

The St James Women Take Heart (WTH) Project comprises a volunteer cohort of women from the greater Chicago metropolitan area who responded to advertisements on television news and print media to participate in a study of heart disease in women during 1992. The target study enrollment was 5000. Inclusion criteria were age 35 years or older, a lack of symptomatic CAD, and the ability to walk on a treadmill at a moderate pace. Women were excluded if they had had typical anginal symptoms or myocardial infarction within the previous 3 months, had blood pressures of ≥170/110 mm Hg before initiating the stress test, weighed >325 pounds (because of equipment limitations), or were pregnant; 5932 women met the inclusion criteria and were examined between May and July of 1992.

Our study-specific exclusion criteria excluded those who underwent a modified Bruce protocol stress test (n=109), because submaximal exercise testing does not accurately reflect physical fitness in the way that maximal exercise testing does.[16] Women with self-reported CAD, previous percutaneous coronary angioplasty, coronary artery bypass graft, or congestive heart failure were also excluded from this analysis (n=91). We excluded 11 women because of incomplete data concerning cardiac risk factors.

After obtaining informed consent, participants provided data on demographics, lifestyle, behavioral variables, and medical history by self-administered questionnaire. Registered nurses performed physical examinations, which included height, weight, waist and hip measurements, blood pressure, radial pulse rate, and auscultation of the heart and lungs. Body mass index was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured by standard clinical procedures.[17] Random urine and nonfasting blood samples were collected for laboratory analysis. Findings suggestive of congestive heart failure, valvular disease, or peripheral vascular disease were referred to the attending cardiologist. During the recording of the resting ECG, supine blood pressures were measured by cardiac technicians. Standing blood pressures were recorded before the stress test.

Framingham Risk Score

The Framingham Risk Score (FRS) has been described previously.[18] The scoring for women is calculated by using a point system for total cholesterol, HDL, age, systolic blood pressure, diastolic blood pressure, the presence or absence of diabetes mellitus, and current smoking. The score ranges between −17 and +25, with higher scores indicating more cardiac risk factors.

We defined diabetes as either self-reported diabetes or nonfasting glucose level of ≥11 mmol/L.[19]

Exercise Testing

Participants underwent a symptom-limited treadmill test according to the Bruce protocol with exercise ECG measurements.[20,21] Heart rate and blood pressure were measured, and a 12-lead ECG was recorded before exercise, at the end of each exercise stage, at peak exercise, and at 1-minute intervals during recovery. The test was discontinued for limiting symptoms (angina, dyspnea, and fatigue), abnormalities of rhythm or blood pressure, or marked and progressive ST-segment deviation. Target heart rates were not used as a predetermined end point.

Exercise capacity is expressed in units of metabolic equivalents (MET) and is an estimate of the maximal oxygen uptake for a given workload.[22] A MET is a measure of ventilatory oxygen consumption expressed as multiples of basal resting requirements, where 1 MET is 1 unit of basal oxygen consumption, which equals 3.5 mL oxygen consumption per kilogram of body weight per minute for an average adult. The exercise capacity (in MET) is estimated by the speed and grade of the treadmill.[23]

TABLE 1. Baseline Characteristics

Characteristic	All Subjects (n=5721)
Age, years	52.4±10.8
Race, %	
White	85.5
African American	9.5
Other*	6
Body mass index, kg/m^2	27.4±5.7
Total cholesterol, mmol/L	5.62±1.07
HDL, mmol/L	1.35±0.39
Hypertension†, %	45.1
Diabetes‡, %	4.9
Smoking, %	
Never	79.4
Current	15.2
Former	5.4
FRS, points	6±6
Exercise capacity, MET	8.0±2.7
Resting heart rate, bpm	79±12
Resting systolic blood pressure, mm Hg	129±19
Resting diastolic blood pressure, mm Hg	82±11
Peak heart rate, bpm	160±16
ST depression ≥1.0 mm, %	6.1

Values are mean±SD or percentage.

*"Other" race category includes those with no stated race.

†Hypertension is defined as history of hypertension or resting systolic blood pressure ≥140 mm Hg or resting diastolic blood pressure ≥90 mm Hg.

‡Diabetes is defined as history of diabetes or nonfasting glucose >11 mmol/L (200 mg/dL)

Follow-Up

All-cause death was used as the end point. Deaths were identified by use of a National Death Index search, matching on date of birth and Social Security number and including all deaths through the year 2000.

Statistical Analyses

Descriptive analyses of all variables were examined. Population characteristics between those who met the primary end point (all-cause death) and the remaining participants were compared by using the χ^2 test for categorical variables or the t test for continuous variables (2-sided). Exercise capacity (in MET) was modeled as a continuous variable and categorical variable. Exercise capacity was stratified as <5 MET, 5 to 8 MET, or >8 MET. This categorization was based on prior studies that showed decreased survival among those who achieved <5 MET and increased survival among those who are able achieve >8 MET when estimated either from exercise activities or a stress test.[5,12,24]

Person-time was calculated for each woman from date of test to date of death from any cause or December 31, 2000, whichever came first. Survival analysis was performed by means of Cox proportional-hazards regression models to determine the effect of exercise capacity on all-cause death, with exercise capacity analyzed as a continuous variable, adjusted for the FRS (as a continuous variable). Analysis of survival within the FRS tertiles for this cohort was performed with the use of the Cox proportional-hazards regression model. Survival was compared by categories of exercise capacity by means of Kaplan-Meier curves. The Cox proportional-hazards assumption was confirmed by visual inspection of the log(−log[survival]) curves. Statistical analyses were performed with the use of STATA 7.0.

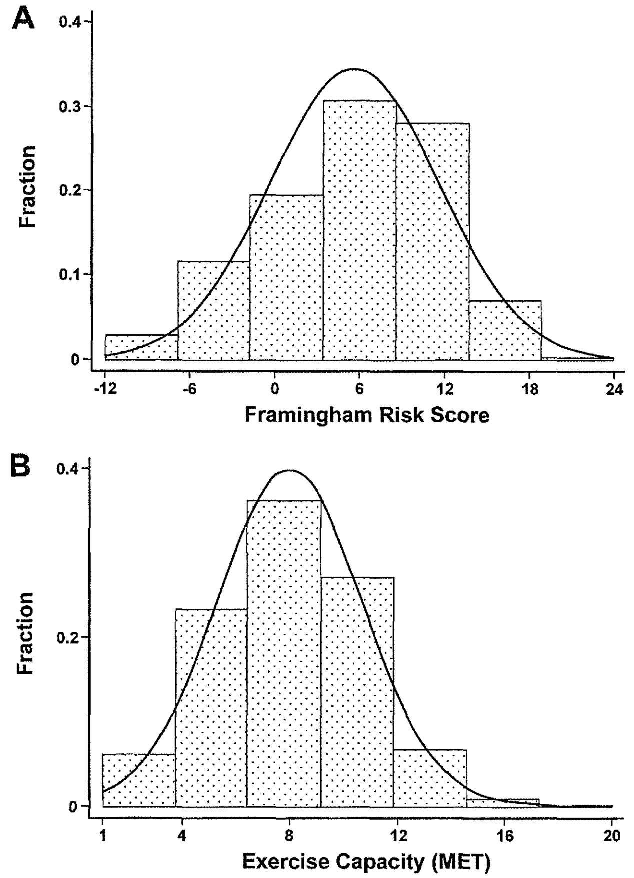

Figure 1. A, Distribution of the FRS (measured by point system) for the cohort. B, Distribution of exercise capacity (in MET) achieved with stress testing for the cohort.

TABLE 2. Characteristics of Those Who Survived Compared With Those Who Died

Characteristic	Survived (n=5541)	Died (n=180)	*P* Value
Age, y	52.2±10.6	62.3±10.9	<0.0001
Race, %			
White	85.4	88.5	0.25
African-American	9.7	6.1	0.11
Other	4.9	5.4	0.76
Body mass index, kg/m^2	27.4±5.8	27.1±5.3	0.58
Resting heart rate, bpm	79±12	81±14	0.085
Hypertension†, %	45	59	<0.0001
Systolic blood pressure, mm Hg	129±25	138±21	<0.0001
Diastolic blood pressure, mm Hg	82±11	82±11	0.37
Current smoking history, %	15.1	20.3	0.052
Diabetes‡, %	4.8	8.8	0.013
Total cholesterol, mmol/L	5.61±1.07	5.68±1.12	0.44
HDL, mmol/L	1.34±0.38	1.31±0.40	0.24
ST depression ≥1.0 mm, %	6.1	6.1	0.99
FRS, points	6±6	9±5	<0.0001
Mean exercise capacity, MET	8.0±2.7	6.2±2.5	<0.0001

Definitions are as in Table 1.

Results

Participant Characteristics

Study population characteristics are given in Table 1. A total of 5721 women met the inclusion criteria for this analysis. This was a predominantly white cohort (85.5%); 9.5% were black. The mean body mass index was 27.4±5.7 kg/m^2. During the follow-up period, 3.2% (n=180) died. The mean (±SD) survival time was 8.4±0.67 years.

The calculated FRS was normally distributed for this population, with a mean FRS of 6±6 U. The scores ranged from −12 to 20 U (Figure 1A). Comparing the surviving population with those who died, there was a statistically significant lower FRS in those alive than in those who died (mean FRS, 6±6 versus 9±5, $P<0.0001$) (Table 2). FRS tertiles strongly predicted survival in this cohort in Cox proportional-hazards regression (Figure 2A). The hazards ratios of death (with 95% CI) for the second and third tertiles compared with the first tertile (those with the lowest FRS) are 3.2 (1.9 to 5.4) and 6.7 (4.1 to 11.1), respectively ($P\leq0.001$). For each increasing tertile, the FRS predicts the 10-year CAD risk to be ≤3%, 4% to 8%, and ≥9%, respectively.[18]

Exercise Test Results

The mean exercise capacity achieved was 8.0±2.7 MET. The distribution of the exercise capacity achieved in this cohort was normally distributed and ranged from 1.5 to 20.0 MET (Figure 1B). The mean exercise capacity achieved by those who died was significantly lower than that of the survivors (6.2±2.5 MET versus 8.0±2.7 MET, $P<0.0001$) (Table 2). Only 22% of those who died achieved the highest exercise capacity category (>8 MET) compared with 50% of those who survived ($P<0.001$); 6.1% of the cohort had significant ST-segment depression (≥1 mm), and the presence of ST-segment depression did not differ between those who survived and those who died (Table 2).

Predictors of Death

The FRS and exercise capacity achieved with stress testing are independent predictors of death, when included in the same model (Table 3). This analysis was not adjusted for age, because the FRS includes age and the correlation between age and the FRS was very high ($r=0.74$). There was no significant interaction between exercise capacity and the FRS (data not shown).

For every increase in exercise capacity by 1 MET, the risk of death was reduced by 17% ($P<0.001$). Similarly, for every unit increase in the FRS, the risk of death increased by 9% ($P<0.001$). Because a lower exercise capacity may reflect subclinical disease, an analysis was performed in which women with early deaths (deaths before the 5th year) were excluded (not shown). The association between exercise capacity, the FRS, and death remained the same.

The survival curves for this cohort by exercise capacity categories, after adjusting for the FRS, are shown in Figure 2B. When compared with the >8 MET group, there were significant differences in the mortality rate among the categories, in which the hazards ratio of death (with 95% CI) was 1.9 (1.3 to 2.9) for the 5- to 8-MET group ($P=0.002$) and 3.1

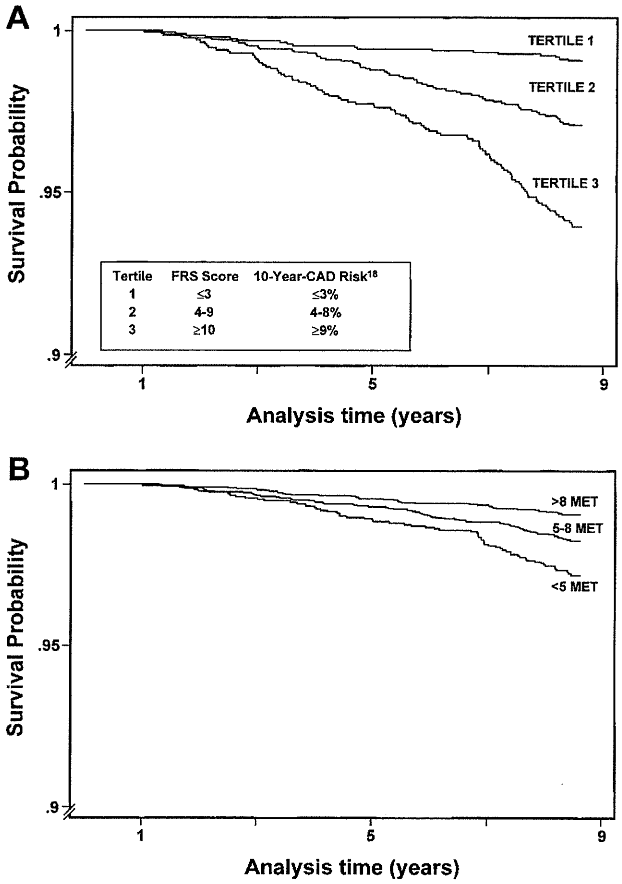

Figure 2. A, Kaplan-Meier survival curves for FRS tertiles. FRS tertiles are measured in points and categorized into tertile 1 (FRS ≤3), tertile 2 (FRS 4 to 9), and tertile 3 (FRS ≥10). The survival rate significantly decreased for each advancing FRS tertile ($P\leq0.001$) when compared with tertile 1 (least cardiac risk factors). B, Kaplan-Meier survival curves for exercise capacity achieved on stress test at baseline, adjusted for FRS. Exercise capacity measured in units of MET and categorized as <5, 5 to 8, and >8 MET. Stratification between MET categories was based on the fact that the groups had distinctly different mortality rates ($P\leq0.002$) after adjusting for FRS.

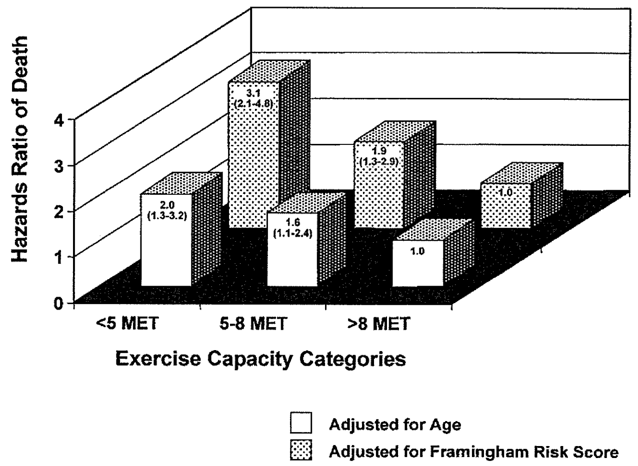

Figure 3. Hazards ratios of all-cause death when adjusted for age (white bars) and FRS (gray bars) for each of the exercise capacity categories (in MET) <5, 5 to 8, and >8. The highest exercise capacity category (>8 MET) was the reference category. Hazards ratios are listed within the bars; 95% CIs are shown in parentheses.

(2.1 to 4.8) for the <5-MET group ($P\leq0.001$). Adjustment for the FRS strengthened the association between exercise capacity and death (Figure 3).

Discussion

We have shown that exercise capacity is a strong independent predictor of all-cause death in asymptomatic women, after adjusting for traditional cardiac risk factors. For each unit (1 MET) increase in exercise capacity, there was a 17% reduction in mortality rate.

Our data confirm the protective role of higher exercise capacity, even in the presence of established cardiac risk factors. Within this cohort of asymptomatic women, the risk of death doubled for those in the 5- to 8-MET exercise capacity category and tripled for those in the lowest (<5 MET) category when compared with the highest exercise capacity category and adjusted for the FRS.

TABLE 3. Hazards Ratio of Death of Independent Predictors of Mortality

	Hazards Ratio	95% CI	*P* Value
Exercise capacity (for each 1-MET increment)	0.83	0.78–0.89	<0.001
FRS (for each unit increment)	1.09	1.05–1.13	<0.001

The FRS[18] and the Framingham Point Score (used in the Adult Treatment Panel III [ATP III] Report)[19] are models used to predict the risk of cardiac disease in women. Both use a point system based on the presence or absence of cardiac risk factors to predict future cardiac events. These models, developed from the Framingham Heart Study[25] and the Framingham Offspring Study,[26] sum points for age, blood pressure, smoking status, total cholesterol (or LDL), and HDL. The difference between them is that the FRS incorporates diabetes into its score,[18] whereas the ATP III guidelines state that the presence of diabetes is a cardiovascular disease equivalent.[19] These prediction models are useful primary prevention devices that can estimate a person's likelihood of future cardiac events, but neither model includes physical fitness (or lack thereof) as a cardiac risk factor within their model.

Our findings confirm that physical fitness, as measured by exercise capacity, is an independent risk factor for death in addition to other cardiac risk factors in asymptomatic women. Previous studies that have described this relation either did not include women[4,5,7,10,27] or lacked the power to draw independent conclusions about women.[6,12] Myers et al[5] prospectively examined >6000 symptomatic men for a mean of 6.2 years. They found that for each 1-MET increase in exercise capacity, there was a 12% reduction in all-cause mortality rate. This study demonstrated the importance of physical fitness for symptomatic men, but our data show that exercise capacity is even more predictive in asymptomatic women.

Epidemiologic studies have noted that exercise capacity is an independent predictor of cardiovascular events and all-cause death in men.[4–12,15] The Lipid Research Clinics Trial[4] and the Aerobics Center Longitudinal Study[7,10] were able to demonstrate the association between physical fitness and death in asymptomatic men. Exercise scores that have been found to predict future cardiac events and death have included the duration of exercise (as a marker of exercise capacity) in the score, including the widely used Duke Treadmill Score.[24,28–30]

The only study before the St James WTH Project that included asymptomatic women comes from the Cooper Clinic.[15] Stress testing was performed on persons presenting for a preventive medical examination, including 3120 women. They found a trend of increased survival for women achieving higher exercise capacity levels, but only the lowest fitness quintile was significantly different from the highest four quintiles combined, after adjusting for cardiac risk factors. In contrast to our study, this study excluded those with diabetes, hypertension, an abnormal ECG (either at rest or with exercise), or inability to achieve 85% age-predicted heart rate. The restrictive exclusion criteria limit the generalizability of their findings. The St James WTH Project only excluded women who had a history of heart disease; target heart rate was not an end point of our stress testing. Our analysis confirms the trend seen in that study and is the first to demonstrate the association between exercise capacity and death in asymptomatic women.

There is significant evidence showing that decreased physical activity is associated with cardiac events and death in both men and women.[25,27,31,32] Unlike physical fitness, which can be objectively measured, physical activity is a behavior, and how well it correlates with exercise capacity has not been extensively validated.[16,33–36] Two studies that focused on women were based on the Framingham Heart Study[32] and the Women's Health Initiative (WHI) Observational Study.[31] The Framingham Heart Study demonstrated a relation between physical activity and all-cause death. The WHI Observational Study was able to show an association between physical activity and cardiac events but concluded that women who engaged in both walking and vigorous activity for at least 2.5 hours per week carried a similar risk reduction of cardiac events when compared with less active women. In both studies, physical activity was assessed by a questionnaire and was essentially an estimate of activity status. Maximal exercise testing is an objective measure of physical fitness and is more readily quantifiable than assessment of physical activity.[16,34]

There are limitations to our study. The voluntary nature of the cohort and the method by which women were recruited affected the demographic makeup of the cohort. Although the participants do not represent a random sample of women from the greater Chicago metropolitan area, estimates of the direction and strength of associations between the physiological variables of interest in this study should be valid for similar, community-dwelling populations of adult women in the United States seen in primary care settings, the population of interest. Also, exercise capacity was measured by using the speed and grade of the treadmill rather than by directly measuring the oxygen consumption, which is more accurate.[37] Finally, our regression analyses demonstrate an association between exercise capacity and all-cause death, not causation. Nonetheless, it is clear that exercise capacity is a marker for risk of death.

The implications of our findings for clinical practice and health care policy are far reaching. The AHA and other such organizations want to find a noninvasive screening test that can predict cardiac risk in asymptomatic individuals to target primary prevention efforts.[38,39] Currently, the ACC/AHA and other experts do not recommend using the standard exercise test for screening in asymptomatic individuals.[3,40] However, our study has demonstrated the added value of stress testing asymptomatic women to assess a woman's risk of death, in addition to traditional cardiac risk factors. We have demonstrated a clear clinical rationale for routine stress testing in asymptomatic women. Furthermore, the achieved exercise capacity should be interpreted and translated to the patient to provide important prognostic information.

Although our study did not test the hypothesis that improved physical fitness through training might improve prognosis, it is interesting to speculate that it might. A prospective study of 9777 asymptomatic men given a stress test at baseline and 5 years after found that individuals who either maintained or improved their exercise capacity had significantly lower all-cause and cardiovascular mortality rates than the "persistently unfit" men. Importantly, this study demonstrated a 7.9% decrease in all-cause mortality rate in men for an increase in treadmill time of $\approx$1 MET.[10] In myocardial infarction survivors followed for 19 years, an increased exercise capacity of 1 MET was associated with an 8% to 14% reduction in mortality rate.[41] High levels of physical fitness, as reflected by the exercise capacity achieved on a maximal stress test, have been shown to be protective of all-cause death in asymptomatic women.

Whether exercise capacity can be easily translated into a level of physical activity is still unknown and is an area in need of further research. Currently, the Surgeon General,[42] the American College of Sports Medicine, the Centers for Disease Control and Prevention,[43] and the AHA[44] recommend that everyone should engage in a physically active lifestyle and that adults should perform moderately intense physical activity for at least 30 minutes per day, preferably every day. In the absence of specific data about the relation between physical activity and exercise capacity, continuing to encourage current physical activity recommendations seems appropriate.

The St James WTH Project confirms that exercise capacity is an independent predictor of death in asymptomatic women, even greater than that previously established among men.[5,10] We were able to show a 17% reduction in mortality rate for every 1-MET increase in exercise capacity. Our findings strongly suggest that in addition to targeting traditional cardiac risk factors as part of the primary prevention evaluation, we must also evaluate the exercise capacity achieved on a maximal stress to fully assess a woman's prognosis.

Acknowledgments

This study was supported by grants from AstraZeneca, DuPont Pharmaceuticals, the Irwin Foundation, Merck, Pfizer/Pharmacia, Siemans-Gammasonics, and St James Hospital. We acknowledge Dr Arfan Al-Hani, who designed the St James WTH Project. Without his foresight, enthusiasm, and dedication, this study would not exist.

His death is a loss to the investigators and participants of this study, as well as to the medical community at large. We are also indebted to the participants of the St James WTH Project, whose continued contribution to the study of heart disease in women is immeasurable.

References

1. Wenger NK, Speroff L, Packard B. Cardiovascular health and disease in women. *N Engl J Med.* 1993;329:247–256.
2. Shaw LJ, Miller DD, Romeis JC, et al. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. *Ann Intern Med.* 1994;120:559–566.
3. Gibbons RJ, Balady GJ, Timothy Bricker J, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *J Am Coll Cardiol.* 2002;40:1531–1540.
4. Ekelund LG, Haskell WL, Johnson JL, et al. Physical fitness as a predictor of cardiovascular mortality in asymptomatic North Am men: the Lipid Research Clinics Mortality Follow-up Study. *N Engl J Med.* 1988; 319:1379–1384.
5. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med.* 2002;346: 793–801.
6. Weiner DA, Ryan TJ, Parsons L, et al. Long-term prognostic value of exercise testing in men and women from the Coronary Artery Surgery Study (CASS) registry. *Am J Cardiol.* 1995;75:865–870.
7. Wei M, Kampert JB, Barlow CE, et al. Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *JAMA.* 1999;282:1547–1553.
8. Slattery ML, Jacobs DR Jr. Physical fitness and cardiovascular disease mortality: the US Railroad Study. *Am J Epidemiol.* 1988;127:571–580.
9. Peters RK, Cady LD Jr, Bischoff DP, et al. Physical fitness and subsequent myocardial infarction in healthy workers. *JAMA.* 1983;249: 3052–3056.
10. Blair SN, Kohl HW III, Barlow CE, et al. Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. *JAMA.* 1995;273:1093–1098.
11. Wyns W, Musschaert-Beauthier E, van Domburg R, et al. Prognostic value of symptom limited exercise testing in men with a high prevalence of coronary artery disease. *Eur Heart J.* 1985;6:939–945.
12. Roger VL, Jacobsen SJ, Pellikka PA, et al. Prognostic value of treadmill exercise testing: a population-based study in Olmsted County, Minnesota. *Circulation.* 1998;98:2836–2841.
13. Cole CR, Blackstone EH, Pashkow FJ, et al. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med.* 1999; 341:1351–1357.
14. Blair SN, Kampert JB, Kohl HW III, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA.* 1996; 276:205–210.
15. Blair SN, Kohl HW III, Paffenbarger RS Jr, et al. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA.* 1989;262:2395–2401.
16. Haskell WL, Leon AS, Caspersen CJ, et al. Cardiovascular benefits and assessment of physical activity and physical fitness in adults. *Med Sci Sports Exerc.* 1992;24:S201–S220.
17. Recommendations for human blood pressure determination by sphygmomanometers. *Circulation.* 1988;77(suppl):501A-514A.
18. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation.* 1998;97:1837–1847.
19. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001;285:2486–2497.
20. Ellstad MH. *Stress Testing: Principles and Practice.* Philadelphia, Pa: FA Davis; 1995.
21. Schlant RC, Blomqvist CG, Brandenburg RO, et al. Guidelines for exercise testing: a report of the Joint Am College of Cardiology/Am Heart Association Task Force on Assessment of Cardiovascular Procedures (Subcommittee on Exercise Testing). *Circulation.* 1986;74(suppl):653A-667A.
22. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *Am Heart J.* 1973;85:546–562.
23. American College of Sports Medicine. *ACMS's Guidelines for Exercise Testing and Prescription.* Baltimore, Md: Lippincott Williams & Wilkins; 2000:368.
24. Mark DB, Shaw L, Harrell FE Jr, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. *N Engl J Med.* 1991;325:849–853.
25. Kannel WB, Feinleib M, McNamara PM, et al. An investigation of coronary heart disease in families: the Framingham offspring study. *Am J Epidemiol.* 1979;110:281–290.
26. Anderson KM, Wilson PW, Odell PM, et al. An updated coronary risk profile: a statement for health professionals. *Circulation.* 1991;83: 356–362.
27. Paffenbarger RS Jr, Hyde RT, Wing AL, et al. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med.* 1986;314: 605–613.
28. Hollenberg M, Zoltick JM, Go M, et al. Comparison of a quantitative treadmill exercise score with standard electrocardiographic criteria in screening asymptomatic young men for coronary artery disease. *N Engl J Med.* 1985;313:600–606.
29. Mark DB, Hlatky MA, Harrell FE Jr, et al. Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med.* 1987; 106:793–800.
30. Shaw LJ, Peterson ED, Shaw LK, et al. Use of a prognostic treadmill score in identifying diagnostic coronary disease subgroups. *Circulation.* 1998;98:1622–1630.
31. Manson JE, Greenland P, LaCroix AZ, et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med.* 2002;347:716–725.
32. Sherman SE, D'Agostino RB, Cobb JL, et al. Physical activity and mortality in women in the Framingham Heart Study. *Am Heart J.* 1994; 128:879–884.
33. Gotay CC. Patient-reported assessment versus performance-based tests. In: Spilker B, ed. *Quality of Life and Pharmacoeconomics in Clinical Trials.* Philadelphia, Pa: Lippincott-Raven Publishers; 1996:413–420.
34. Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? *Med Sci Sports Exerc.* 2001; 33:S379–S399; discussion S419–S420.
35. Blair SN, Jackson AS. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Med Sci Sports Exerc.* 2001;33: 762–764.
36. Bairey Merz CN, Olson M, McGorray S, et al. Physical activity and functional capacity measurement in women: a report from the NHLBI-sponsored WISE study. *J Womens Health Gend Based Med.* 2000;9: 769–777.
37. Myers J. *Essentials of Cardiopulmonary Exercise Testing.* Champaign, Ill: Human Kinetics; 1996.
38. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS: Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA.* 1998;279:1615–1622.
39. Mitka M. AHA addresses atherosclerosis testing: American Heart Association. *JAMA.* 1999;282:1991–1992.
40. Froelicher VF, Fearon WF, Ferguson CM, et al. Lessons learned from studies of the standard exercise ECG test. *Chest.* 1999;116:1442–1451.
41. Dorn J, Naughton J, Imamura D, et al. Results of a multicenter randomized clinical trial of exercise and long-term survival in myocardial infarction patients: the National Exercise and Heart Disease Project (NEHDP). *Circulation.* 1999;100:1764–1769.
42. Physical activity and health: a report of the Surgeon General. Atlanta: Department of Health and Human Services, Center for Disease Control and Prevention, National Center for Disease Prevention and Health Promotion, 1996.
43. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA.* 1995;273: 402–407.
44. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation.* 2001;104:1694–1740.

論文名	Exercise capacity and the risk of death in women: the St James Women Take Heart Project						
著者	Gulati M, Pandey DK, Arnsdorf MF, Lauderdale DS, Thisted RA, Wicklund RH						
雑誌名	Circulation						
巻・号・頁	108(13)巻　1554-1559ページ						
発行年	2003						
PubMedリンク	http://www.ncbi.nlm.nih.gov/pubmed/12975254						
対象の内訳		ヒト	動物	地域	欧米	研究の種類	縦断研究
	対象	一般健常者	空白		( )		コホート研究
	性別	女性	( )		( )		( )
	年齢	平均年齢52.4歳			( )		前向き研究
	対象数	5000～10000	空白		( )		( )
調査の方法	実測	( )					
アウトカム	予防	なし	なし	なし	なし	(死亡)	( )
	維持・改善	なし	なし	なし	なし	( )	( )
図表							
図表掲載箇所							
概要（800字まで）	背景：心血管疾患は、女性における主な死亡原因であり、それは半数よりも多い。心血管疾患におけるほとんどの研究で、女性を対象としたものは少ない。男性においては、減少した体力は、死亡リスクを増加させることが知られている。運動負荷テストによって測定される運動能力は、体力の客観的な測定値である。減少する運動能力が死亡リスクの増加に関連しているという仮説が、1992年のベースライン時にテストを受けた5721名の無症状の女性コホートで調査された。方法と結果：ベースライン時で集められた情報は、検診と家族歴、人口統計の特性、体力テスト、およびBruce protocolを用いた症候限界による負荷心電図であった。運動能力は代謝当量（MET）により評価された。絶食状態でない血液は、ベースライン時で分析された。National Death Index検索が、2000年の終わりまで全死亡原因とその死亡の日付を特定するために行われた。ベースライン時における参加者の平均年齢（±標準偏差）は52±11であった。Framingham Risk Scoreにより補正された死亡の危険比（95%信頼区間として）は、METsレベル5以下、5-8、および8以上でそれぞれ3.1（2.0-4.7）、1.9（1.3-2.9）、および1.00であった。Framingham Risk Scoreにより補正された死亡リスクは、1-MET増加毎に17%減少した。結論：本研究は、このような関連研究でも最も長い追跡調査にわたり研究された無症状の女性に対する最大のコホートである。また、本研究は運動能力が無症状の女性の死亡の独立予測因子であることを確認しており、先行研究において男性で確立されたことより優れた結果である。						
結論（200字まで）	女性の場合、心肺体力の水準に応じて段階的に総死亡リスクは低下する。						
エキスパートによるコメント（200字まで）	女性を対象に、最大酸素摂取量と死亡リスクとの関連について検討した少ない研究の一つ。						

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Scand J Work Environ Health 2010;36(5):357–365

Physical demands at work, physical fitness, and 30-year ischaemic heart disease and all-cause mortality in the Copenhagen Male Study

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Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Physical demands at work, physical fitness, and 30-year ischaemic heart disease and all-cause mortality in the Copenhagen Male Study. *Scand J Work Environ Health.* 2010;36(5):357–365.

Objective No previous long-term prospective studies have examined if workers with low cardiorespiratory fitness have an increased risk of cardiovascular mortality due to high physical work demands. We tested this hypothesis.

Method We carried out a 30-year follow-up of the Copenhagen Male Study of 5249 employed men aged 40–59 years. We excluded from follow-up 274 men with a history of myocardial infarction, prevalent symptoms of angina pectoris, or intermittent claudication. We estimated physical fitness [maximal oxygen consumption (VO_2Max)] using the Åstrand cycling test and determined physical work demands with two self-reported questions.

Results In the Copenhagen Male Study, 587 men (11.9%) died due to ischaemic heart disease (IHD). Using men with low physical work demands as the reference group, Cox analyses – adjusted for age, blood pressure, smoking, alcohol consumption, body mass index, diabetes, and hypertension – showed that high physical work demands were associated with an increased risk of IHD mortality in the least fit [VO_2Max range 15–26, N=892, hazard ratio (HR) 2.04, 95% confidence interval (95% CI) 1.20–3.49] and moderately fit (VO_2Max range 27–38, N=3037, HR 1.75, 95% CI 1.24–2.46), but not among the most fit men (VO_2Max range 39–78, N=1014, HR 1.08, 95% CI 0.52–2.17). We found a similar, although slightly weaker, relationship with respect to all-cause mortality.

Conclusions The hypothesis was supported. Men with low and medium physical fitness have an increased risk of cardiovascular and all-cause mortality if exposed to high physical work demands. Ours observations suggest that, among men with high physical work demands, being physically fit protects against adverse cardiovascular effects.

Key terms cardiovascular health; occupational health; occupational physical activity.

In a recent paper, Krause and colleagues (1) addressed the fact that the literature on the role of occupational physical activity as a risk factor for ischaemic heart disease (IHD) is conflicting, and that only a small number of studies have included information on both leisure-time and occupational physical activity.

In the Copenhagen Male Study, we found that, in contrast to physical activity during leisure time, exposure to high physical work demands is associated with an increased risk of IHD and all-cause mortality (2). Furthermore, we showed that a moderate or high level of physical activity during leisure time was associated with a lower risk of IHD and all-cause mortality irrespective of the level of physical demands at work (2).

It is well established that being sedentary during leisure time is associated with an increased risk of premature mortality (3, 4), so promoting physical activity during leisure time is recommended (5). Physical training rapidly increases physical fitness (6). Low physical fitness is an independent predictor of IHD and premature mortality (7–10). Physical fitness determines cardiovascular workload at any given level of physical work intensity (11). In other words, the lower the cardiorespiratory fitness a worker possesses, the higher

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his cardiovascular workload will be when performing a physically demanding work task.

Two long-term cohort studies from Finland (1, 12) reported that, in contrast to energy expenditure during leisure-time physical activity, high energy consumption at work may have detrimental effects on cardiovascular health even when controlling for the level of physical activity during leisure time and other well-known risk factors for IHD. To our knowledge, no previous study, apart from that of Krause and colleagues (1), has concomitantly taken into account information on physical activity during leisure time and used an objective measure of physical fitness when studying the association of occupational physical work demands with risk of IHD. As an endpoint, Krause's study (1) used the carotid intima-media thickness, which is a reliable surrogate marker of coronary atherosclerosis and also an independent predictor of manifest coronary heart disease.

No previous long-term prospective studies have examined if workers with low cardiorespiratory fitness have an increased risk of cardiovascular mortality due to high physical work demands. We tested this hypothesis.

Methods

Study population

The Copenhagen Male Study was established in 1970–1971 and comprised 5249 (87% of those invited to participate) male employees, aged 40–59 years, from 14 companies, covering the railway, public road construction, military, postal, telephone, customs, national bank, and medical industry sectors (13, 14).

The examination consisted of a questionnaire, a short interview, and a clinical examination including measurements of height, weight, and blood pressure. Indirect measurement of physical fitness [maximal oxygen consumption (VO_2Max)] was performed with a bicycle ergometer. Thirty-five men with orthopaedic problems, who were unable to perform the bicycle test, were excluded from the study.

From the questionnaire, we obtained information about working conditions, lifestyle, and general health, including history of myocardial infarction, angina pectoris, and intermittent claudication. The information given in the questionnaire was clarified with each subject in the ensuing interview. Details on the questionnaire have already been published (15). A number of these factors are elaborated in more detail below.

Eligibility

In addition to the 35 men unable to carry out the bicycle test, men with a history of myocardial infarction (N=74), angina pectoris (N=165) or intermittent claudication (N=105) were excluded from the prospective study. In total, the excluded group comprised these 274 men and 9 men with missing answers, leaving 4943 men for the incidence study. With respect to all variables included, missing values ranged from 0–2.7%.

Physical fitness

Heart rate was measured during submaximal bicycle work in a steady state with the aid of a stopwatch and stethoscope. The loads used were 100, 150, and 200 W. One, two, or in a few cases, three different loads were used. The load chosen in each case was determined by the weight and age of the person or heart rate during the first minute of the test; we determined the VO_2Max using Åstrand's nomogram (6). The correlation between directly and indirectly measured VO_2Max is high. The method used has previously been described in detail (13).

Physical activity at work, general description

Physical activity during work was estimated by the following question: "Which description most precisely covers your pattern of physical activity at work?" Groups were defined according to the following responses: (i) You are mainly sedentary and do not walk much around at your workplace, for example, desk work, and work including assembling of minor parts (group 1); (ii) You walk around quite a bit at your workplace but do not have to carry heavy items, eg, light industrial work, non-sedentary office work, inspection and the like (group 2); (iii) Most of the time you walk, and you often have to walk up stairs and lift various items. Examples include mail delivery and construction work (group 3); (iv) You have heavy physical work. You carry heavy burdens and carry out physically strenuous work, eg, work including digging and shoveling (group 4). In the analyses, physical activity was defined as follows: group 1=low, group 2=medium; group 3=high (since only 2.4% belonged to group 4, groups 3 and 4 were pooled) and are referred to as high.

Strenuous work

Strenuous work was estimated from the question: "Do you perform strenuous work (work resulting in sweating)?" The answer options were: "often", "occasionally", and "seldom or never" and coded as follows: 1=seldom or never, 2=occasionally, and 3=often.

Physical work activity, combined variable

An additional variable was constructed in order to further distinguish between the presence or absence of physically demanding work. Summing up the values from the aforementioned questions on physical activity and strenuous work gave values ranging from 2–6. A low combined score of 2 was defined as "low physical work demands", a score of 3 or 4 was defined as "moderate physical work demands", and a score of 5 or 6 was defined as "high physical work demands".

Physical activity during leisure time

In order to determine this factor, the questionnaire asked "Which description most precisely covers your pattern of physical activity at leisure time?" with the following possible responses: (i) You are mainly sedentary, for example, you read, watch television, go to the cinema. In general you spend most of your leisure time performing sedentary tasks (group 1); (ii) You go for a walk, use your bicycle a little or perform activity for at least 4 hours per week, for example, light gardening, leisure-time building activity, table tennis and bowling (group 2); (iii) You are an active athlete, eg, run or play tennis or badminton for at least 3 hours/week. If you frequently perform heavy gardening, you also belong to this group (group 3); (iv) You take part in competitive sports, swim, play European football, handball or run long distances regularly several times per week (group 4).

In the analyses, the level of physical activity during leisure time was defined as group 1=low, group 2=moderate, and group 3=high (since only 0.4% belonged to group 4, groups 3 and 4 were pooled).

Lifestyle factors

The male workers reported if they were current smokers, previously smoked, or had never smoked. In addition, participants reported their daily average alcohol consumption as the number of alcoholic beverages consumed per day in the following categories: 0, 1–2, 3–5, 6–10, and >10.

Clinical and health-related factors

Based on height and weight measurements, body mass index (BMI) was calculated as kg/m^2. Blood pressure was measured with the subject seated and after at least five minutes rest. A 12 cm wide, 26 cm long cuff was firmly and evenly applied to the right upper arm with the lower edge of the cuff placed 2 cm antecubitally. Diastolic blood pressure was recorded at the point where the Korotkoff sounds disappeared (phase 5). In addition, the participants were asked if they received treatment for either hypertension or diabetes from their physician or elsewhere. The answer options were yes or no.

Social class

The men were divided into five social classes according to a system originally elaborated by Svalastoga and later adjusted by Hansen (16, 17) This classification system is based on education level and job position in terms of the number of subordinates. Typical jobs in the study cohort were: (i) officer, civil engineer, office executive, or head of department (social class I); (ii) head clerk or engineer (social class II); engine driver or train guard (social class III); machine fitter in a telephone company (social class IV); and unskilled laborer, mechanic, or driver (social class V).

End-points

We obtained information on death diagnoses between the period 1970–1971 to the end of 2001 from official national registers. The IHD mortality diagnoses included International Classification of Diseases' codes ICD-8: 410–14, and (from 1994) ICD-10: I20–I25.

Statistical analysis

We performed basic statistical analyses, Chi-squared analysis (likelihood ratio), analysis of variance, and regression analyses. We estimated relative risks (RR) by exp(β), where β is the hazard coefficient for the variable of interest in a Cox's proportional hazards regression model with the maximum likelihood ratio method. Assumptions regarding the use of Cox's proportional hazards were met by inspection of the log minus log function as the covariate mean. A final Cox proportional hazards regression analyses, with IHD mortality as outcome, was performed to obtain a statistical expression for the conspicuous difference in the predictive value of physical work demands and IHD mortality between men with high and low physical fitness. In addition to the main effects of the two variables (physical fitness and physical work demands), age, lifestyle factors, alcohol consumption, and smoking habits, we included a multiplicative interaction term between physical fitness (highest fifth/others) and the three-group variable depicting the level of physical work demands. We took, a priori, as significant a two-sided probability value of $P<0.05$.

Results

In the eligible study population of male employees who had completed the ergometer test and were without a history of myocardial infarction, angina pectoris, or intermittent claudication, 587 died (11.9%) from IHD during the period 1970/1971–2001. During the same time, 2663 (54.0%) died in total.

Table 1 shows lifestyle and other characteristics of men belonging to groups with different levels of physical fitness (VO_2Max); lowest fifth: range 15–26; three intermediate fifths: range 27–38; and highest fifth: 39–78. The level of physical fitness was inversely associated with systolic and diastolic blood pressure, alcohol consumption, treatment due to hypertension, BMI, and age. No significant relationship was found between the level of fitness and social class. As previously reported, smokers surprisingly had higher levels of physical fitness (13).

Table 2 shows lifestyle and other characteristics of men belonging to different groups of self-assessed leisure-time physical activity. Compared to men with lower levels of physical activity during leisure time, men reporting higher levels were younger, had a higher level of physical fitness and lower systolic and diastolic blood pressure and BMI, while fewer were current smokers, consumed ≥6 alcoholic beverages/day, belonged to low social class, and received treatment for hypertension.

Table 3 shows the lifestyle and other characteristics of men belonging to the different groups of physical activity level at work. We observed a significant positive correlation to physical fitness, although the association was less pronounced than that found between physical activity during leisure time and fitness as presented in table 2. Also the level of occupational physical activity was positively correlated with smoking, alcohol use, BMI, and low social class.

Table 4 shows the association of baseline physical fitness, the level of physical activity during leisure time, and physical work demands with risk of IHD and all-cause mortality. Men with high physical fitness had a 45% lower risk of IHD mortality [age-adjusted hazard ratio (HR) 0.55, 95% confidence interval (95% CI) 0.42–0.73] and a 38% lower risk of all-cause mortality (age-adjusted HR 0.62, 95% CI 0.55–0.71) compared to men with low physical fitness. Also men reporting moderate or high levels of leisure-time physical activity had a lower risk of both IHD and all-cause mortality compared to workers reporting low leisure-time physical activity. Of particular interest was the 50% reduced risk of IHD mortality among men who have a high compared to low level of physical activity during leisure time. In contrast, men with high physical work demands had a 69% increased risk of IHD mortality (age-adjusted HR 1.69, 95% CI 1.31–2.17) and a 51% higher risk of all-cause mortality (age-adjusted HR 1.51, 95% CI 1.34–1.70) compared to men with low physical work demands. The right column of the table shows the result of Cox analyses taking into

Table 1. Lifestyle and other characteristics according to measured physical fitness, maximal oxygen consumption (VO_2Max) among men with no history of myocardial infarction, angina pectoris, or intermittent claudication. [SD=standard deviation; freq=frequency].

	Level of physical fitness									P-value [a]	P-value [b]
	Lowest quintile (N=892) VO_2Max range 15–26			3 medium quintiles (N=3037) VO_2Max range 27–38			Highest quintiles (N=1014) VO_2Max range 39–78				
	Mean	SD	Freq (%)	Mean	SD	Freq (%)	Mean	SD	Freq (%)		
Physical fitness (VO_2Max)	23.5	2.3	·	32.2	3.3	·	43.8	4.8	·	·	·
Lifestyle factors 1970–1971											
Smoker											
Current	·	·	67.6	·	·	71.6	·	·	76.3		
Previous	·	·	23.2	·	·	19.1	·	·	15.4	<0.001	<0.001
Never	·	·	9.2	·	·	9.3	·	·	8.3		
Alcohol, beverages per 24 hours											
0	·	·	31.5	·	·	33.7	·	·	36.1		
1–2	·	·	42.9	·	·	48.3	·	·	41.7	<0.001	<0.001
3–5	·	·	20.8	·	·	14.8	·	·	13.9		
≥6	·	·	4.9	·	·	3.2	·	·	1.3		
Clinical risk factors											
Diabetes (treatment of)	·	·	1.1	·	·	0.7	·	·	0.7	0.34	0.39
Systolic blood pressure (mm Hg)	143.7	20.2		134.5	18.3		127.3	16.3	·	<0.001	0.06
Diastolic blood pressure (mm Hg)	87.2	12.2		82.9	11.2		79.3	10.7	·	<0.001	0.29
Hypertension (treatment of)	·	·	2.4	·	·	1.5	·	·	1.1	0.03	0.09
Body mass index (kg/m²)	26.8	3.4		25.2	2.8		24.1	2.5	·	<0.001	0.03
Other characteristics											
Low social class (classes IV/V)	·	·	56.3	·	·	54.7	·	·	54.7	0.51	0.71
Age (years)	50.8	5.2		48.5	5.3		46.9	4.8	·	<0.001	0.04

[a] P-values of trend test (Kendall's tau B) or test for linearity in analysis of variance.
[b] P-values of Chi-square test or test for deviation in analysis of variance.

Table 2. Physical fitness and other characteristics according to the level of leisure-time physical activity among men with no history of myocardial infarction, angina pectoris, or intermittent claudication. [SD=standard deviation; freq=frequency; VO_2Max=maximal oxygen consumption]

	Level of physical activity during leisure time									P-value [a]	P-value [b]
	Low (N=814)			Medium (N=3514)			High (N=504)				
	Mean	SD	Freq (%)	Mean	SD	Freq (%)	Mean	SD	Freq (%)		
	31.1	6.6	·	33.0	7.0	·	36.9	8.2	·	<0.001	<0.001
Lifestyle factors 1970–1971											
Smoker											
Current	·	·	78.0	·	·	71.1	·	·	65.5		
Previous	·	·	14.9	·	·	19.8	·	·	21.4	<0.001	<0.001
Never	·	·	7.1	·	·	9.1	·	·	13.1		
Alcohol, beverages per 24 hours											
0	·	·	31.1	·	·	34.2	·	·	35.9		
1–2	·	·	42.6	·	·	48.1	·	·	51.0	<0.001	<0.001
3–5	·	·	20.3	·	·	15.2	·	·	10.6		
≥6	·	·	5.9	·	·	2.5	·	·	2.6		
Clinical risk factors											
Diabetes (treatment of)	·	·	1.5	·	·	0.5	·	·	1.0	0.21	0.02
Systolic blood pressure (mm Hg)	135.3	19.7		134.7	18.8		132.5	17.7	·	0.02	0.24
Diastolic blood pressure (mm Hg)	83.8	11.8		83.0	11.4		80.8	10.7	·	<0.001	0.06
Hypertension (treatment of)	·	·	2.1	·	·	1.7	·	·	0.6	0.04	0.06
Body mass index (kg/m^2)	25.6	3.3		25.3	2.9		24.8	2.8	·	<0.001	0.47
Other characteristics											
Low social class (classes IV/V)	·	·	61.8	·	·	54.0	·	·	47.9	<0.001	<0.001
Age (years)	49.3	5.5		48.6	5.2		47.5	5.2	·	<0.001	0.21

[a] P-values of trend test (Kendall's tau B) or test for linearity in analysis of variance.
[b] P-values of Chi-square test or test for deviation in analysis of variance.

account, in addition to age, relevant potential confounders as identified in tables 1–3. As could be expected, the associations were somewhat attenuated for all three predictor variables, but the overall trend remained. In particular, the association of fitness with the risk of IHD mortality was affected by the inclusion of blood pressure variables and yet, the trend persisted.

Table 5 shows the risk of IHD and all-cause mortality during follow-up among men with low, medium, and high physical fitness, stratified according to the level of physical work demands. The results of Cox proportional hazard analyses, including different potentially confounding variables, are presented. Among men with low and medium physical fitness levels, men with high physical work demands had a significantly twofold increased risk of IHD when adjusted for age only. Further adjustment did not materially influence this result. In contrast, among the fittest men, who overall had the lowest risk, no association was found between increasing physical work demands and the risk of IHD mortality.

Among men with the lowest level of physical fitness, those with high physical work demands had a 43% significantly higher risk for all-cause mortality than men with low demands. This difference was attenuated to a non-significant level when controlling for potential confounders. Among men with a medium level of physical fitness, the largest group, those with high physical work demands had a 60% significantly higher risk for all-cause mortality than men with low demands. This difference was also attenuated when controlling for potential confounders but remained statistically significant. Among men with the highest level of physical fitness, those with high physical work demands had a 33% non-statistically significant increased risk of all-cause mortality when controlling for age only. This estimate did not materially change with further adjustment.

In two additional analyses, we further tested the relative importance of physical fitness as an effect modifier for the association between physical work demands and mortality (data not shown). We carried out an age-adjusted Cox analysis including an interaction term between physical work demands and physical fitness level with risk of IHD mortality as the endpoint. When we included smoking habits and alcohol consumption, following a backward elimination procedure, the interaction was highly significant (P=0.002). We also carried out an age-adjusted Cox analysis including an interaction term between physical work demands and physical fitness level with risk of all-cause mortality as the endpoint. When smoking habits and alcohol consumption were included, following a backward elimination procedure, the interaction was not significant (P=0.22).

In the analyses presented in the tables, we pooled the three medium (intermediate) quintiles covering the

Table 3. Lifestyle and other characteristics according to physical work demands based on the combined activity variable (general physical work demands and strenuous work resulting in sweating) among men without history of myocardial infarction, angina pectoris, or intermittent claudication. [SD = standard deviation; VO_2Max = maximal oxygen consumption]

	Physical work demands									P-value [a]	P-value [b]
	Low (N=1239)			Medium (N=2661)			High (N=860)				
	Mean	SD	Frequency (%)	Mean	SD	Frequency (%)	Mean	SD	Frequency (%)		
Physical fitness (VO_2Max)	32.6	7.1	·	33.1	7.3	·	33.9	7.4	·	<0.001	0.69
Leisure-time physical activity											
Low	·	·	18.9	·	·	15.6	·	·	17.2		
Medium	·	·	70.4	·	·	75.2	·	·	69.3	0.07	<0.001
High	·	·	10.7	·	·	9.2	·	·	13.4		
Lifestyle factors 1970–1971											
Smoker											
Current	·	·	66.6	·	·	72.2	·	·	76.4		
Previous	·	·	22.4	·	·	19.0	·	·	15.6	<0.001	<0.001
Never	·	·	11.1	·	·	8.8	·	·	8.0		
Alcohol, beverages per 24 hours											
0	·	·	38.8	·	·	34.3	·	·	25.9		
1–2	·	·	50.8	·	·	47.6	·	·	42.0	<0.001	<0.001
3–5	·	·	9.2	·	·	15.4	·	·	25.1		
≥6	·	·	1.1	·	·	2.8	·	·	7.0		
Clinical risk factors											
Diabetes (treatment of)	·	·	0.9	·	·	0.6	·	·	1.2	0.71	0.19
Systolic blood pressure (mm Hg)	134.8	18.5		134.6	19.0		134.1	19.5	·	0.56	0.73
Diastolic blood pressure (mm Hg)	83.3	11.5		82.8	11.4		82.9	11.7	·	0.30	0.40
Hypertension (treatment of)	·	·	1.9	·	·	1.6	·	·	1.5	0.51	0.78
Body mass index (kg/m²)	24.7	2.8		25.3	3.0		25.9	3.1	·	<0.001	0.86
Other characteristics											
Low social class (classes IV/V)	·	·	21.7	·	·	58.9	·	·	91.3	<0.001	<0.001
Age (years)	48.7	5.3		48.6	5.3		48.6	5.2	·	0.73	0.66

[a] P-values of trend test (Kendall's tau B) or test for linearity in analysis of variance.
[b] P-values of Chi-square test or test for deviation in analysis of variance.

VO_2Max range 27–38. In order to identify a possible threshold value for a protective effect of physical fitness on possibly adverse effects on IHD mortality from high physical work demands, we looked at the risk of IHD associated with work demands within all quintiles (data not shown). Except for the highest quintile (ie, VO_2Max range 39–78), we consistently observed a positive gradient between increasing work demands and IHD risk.

Discussion

Our hypothesis that the level of physical fitness modifies the association between high physical work demands and the risk of IHD mortality was supported. We observed an increased risk of IHD mortality associated with increasing physical work demands among men with low and medium levels of physical fitness that was absent among the most physically fit men. Similar results were found for all-cause mortality, with the possible exception that even the most-fit men who were exposed to high physical work demands had a 25% increased risk of all-cause mortality, although this latter finding was not statistically significant.

Physical work demands, fitness, and IHD mortality

Our study extends the old notion of physical fitness being a critical individual resource, not only for the performance of a physically demanding job (18, 19), but also to survive its effects.

Physical fitness is a well-documented prognostic factor for premature cardiovascular and all-cause mortality (7–10). The findings of a 25% lower risk for IHD mortality and 29% lower risk for all-cause mortality among men with high compared to low physical fitness (table 4) support the importance of physical fitness. Of particular clinical interest was the considerably lower systolic and diastolic blood pressure among men with high versus low physical fitness (systolic blood pressure of 127 versus 144 mmHg and diastolic blood pressure of 79 versus 87 mmHg). Men with high physical work

Table 4. Physical fitness and physical activity during work and leisure time as predictors of ischaemic heart disease and all–cause mortality during 1970–71 to end of 2001 among men without history of myocardial infarction, angina pectoris or intermittent claudication at baseline. [HR = hazard ratio; 95% CI = 95% confidence interval; VO_2Max = maximal oxygen consumption]

	Mortality		Incidence per 100 000 person years	HR [a]	95% CI	HR [b]	95% CI
	N	%					
Ischemic heart disease mortality							
Physical fitness, VO_2Max							
Lowest quintile, 15–26 range (N=892)	148	16.6	719	1.00	.	1.00 [c]	.
Medium quintiles, 27–38 range (N=3037)	354	11.7	468	0.75	0.62–0.91	0.88	0.72–1.09
Highest quintiles, 39–78 range (N=1014)	85	8.4	315	0.55	0.42–0.73	0.75	0.56–1.00
Leisure time physical activity							
Low (N=814)	128	15.7	667	1.00	.	1.00 [d]	.
Moderate (N=3514)	398	11.4	449	0.67	0.55–0.82	0.72	0.58–0.88
High (N=504)	40	8.0	304	0.49	0.34–0.70	0.59	0.41–0.85
Physical work demands							
Low (N=1239)	123	10.0	385	1.00	.	1.00 [e]	.
Moderate (N=2661)	317	11.9	477	1.30	1.05–1.60	1.26	1.02–1.56
High (N=860)	121	14.1	588	1.69	1.31–2.17	1.55	1.19–2.02
All–cause mortality							
Physical fitness, VO_2Max							
Lowest quintile, 15–26 range (N=892)	610	68.5	2962	1.00	.	1.00 [c]	.
Medium quintiles, 27–38 range (N=3037)	1630	53.8	2156	0.81	0.74–0.89	0.87	0.79–0.96
Highest quintiles, 39–78 range (N=1014)	423	41.9	1567	0.62	0.55–0.71	0.71	0.62–0.81
Leisure time physical activity							
Low (N=814)	526	64.6	2742	1.00	.	1.00 [d]	.
Moderate (N=3514)	1845	52.6	2084	0.74	0.67–0.82	0.81	0.74–0.90
High (N=504)	218	43.5	1659	0.62	0.53–0.72	0.74	0.63–0.87
Physical work demands							
Low (N=1239)	598	48.5	1872	1.00	.	1.00 [e]	.
Moderate (N=2661)	1436	54.1	2164	1.22	1.11–1.34	1.17	1.06–1.29
High (N=860)	523	60.8	2543	1.51	1.34–1.70	1.33	1.18–1.51

[a] Adjusted for age.
[b] Fully adjusted.
[c] Adjusted for age, body mass index, systolic and diastolic blood pressure, hypertension (treatment of), alcohol use, smoking (current, never, previous)
[d] Adjusted for age, body mass index, systolic and diastolic blood pressure, hypertension (treatment of), alcohol use, smoking (current, never, previous), occupational physical work demands, physical fitness (VO_2Max)
[e] Adjusted for age, body mass index, alcohol use, smoking (current, never, previous), leisure time physical activity, physical fit–ness (VO_2Max)

demands have previously been reported to have lower levels of physical fitness than men with low physical work demands (ie, sedentary workers) (19). In this study, men with high occupational physical demands had a slightly higher physical fitness compared to those with low physical work demands (33.9 versus 32.6 VO_2Max). In comparison, men reporting a high level of leisure-time physical activity had a much higher physical fitness than men classifying themselves as basically sedentary during leisure time (36.9 versus 31.1 VO_2Max). This finding indicates that high physical work demands generally only have a minor influence on physical fitness, and highlights the significance of physical activity during leisure time for improving the aerobic capacity.

Men with high levels of fitness were observed to have a non-significant enhanced risk (25%) for all-cause mortality from high physical work demands. This finding indicates that men with high physical fitness cannot be excluded from having an enhanced risk for all-cause mortality from high physical work demands. This aspect needs to be further investigated in a larger population among men with high physical fitness.

In this study, we observed that a relatively low proportion of the male employees (~20%) have sufficiently high fitness to protect them from the increased risk for IHD and all-cause mortality resulting from high physical work demands. Previous studies from two Nordic countries (1, 20) have shown that a relatively high proportion of employees (~30%) have an energy expenditure at work that is in excess of the recommended maximum level of occupational aerobic strain (11). A dual prevention strategy, consisting of both fitness-enhancing physical exercise and tailoring of physical work demands with respect to the physical fitness of the employee may, in

Table 5. Physical work demands and risk of ischaemic heart disease (IHD) and all-cause mortality 1970–71 to end of 2001 according to level of physical fitness: lowest quintile, three medium quintiles, and highest quintile. Different adjustment criteria are applied in Cox proportional hazards regression analyses with forced entry of variables. [HR = hazard ratios; 95% CI = 95% confidence intervals]

Physical work demands	IHD mortality					All-cause mortality				
	Crude incidence (%)	HR[a]	95% CI	HR[b]	95% CI	Crude incidence (%)	HR[a]	95% CI	HR[b]	95% CI
Low physical fitness (N=838)										
Low (N=242)	13.7	1.00[c]	·	1.00[c]	·	63.9	1.00[c]	·	1.00[c]	·
Moderate (N=468)	16.5	1.28	0.85–1.93	1.33	0.87–2.03	69.2	1.18	0.97–1.43	1.09	0.89–1.33
High (N=128)	22.7	1.98[d]	1.20–3.26	2.04[d]	1.20–3.49	75.8	1.43[d]	1.11–1.85	1.20	0.91–1.57
Moderate physical fitness (N=2916)										
Low (N=755)	9.0	1.00[c]	·	1.00[c]	·	45.8	1.00[c]	·	1.00[c]	·
Moderate (N=1625)	11.8	1.45[d]	1.10–2.62	1.39[e]	1.05–1.84	54.5	1.33[f]	1.17–1.50	1.25[f]	1.10–1.42
High (N=536)	14.2	1.89[f]	1.39–2.62	1.75[f]	1.24–2.46	62.1	1.60[f]	1.43–1.93	1.45[f]	1.24–1.70
High physical fitness (N=983)										
Low (N=233)	8.7	1.00[c]	·	1.00[c]	·	40.7	1.00[c]	·	1.00[c]	·
Moderate (N=558)	8.3	0.96	0.57–1.62	1.02	0.60–1.76	40.1	1.00	0.79–1.28	1.00	0.78–1.28
High (N=192)	8.3	1.08	0.56–2.09	1.08	0.52–2.17	46.9	1.33	0.98–1.75	1.25	0.92–1.69

[a] Adjusted for age.
[b] Adjusted for all potential confounders: age, body mass index, systolic and diastolic blood pressure, treatment of diabetes or hypertension, alcohol use, and smoking (current, never, previous).
[c] Reference.
[d] P≤0.01.
[e] P≤0.05.
[f] P≤0.001.

theory, reduce the risk of IHD and all-cause mortality among employees with high physical work demands. Neither the individual's fitness level nor the occupational physical work demands are the sole responsibility of the worker. A great potential for prevention may exist by reducing the load of physical work tasks and allowing people with physically demanding work, even after the reduction of the workload, to receive physical training during working hours.

Methodological considerations

A methodological aspect of this study is that the occupational and leisure-time physical activity information was based on self-assessment, which invariably entails some degree of misclassification (21). However, no technical equipment for measuring daily physical activity at work and during leisure time was available in 1970, at least not in Denmark. In addition, the lack of continuous exposure data and repeated measures of exposure during the relatively long follow-up period may have contributed to a misclassification of exposure. The study population of the Copenhagen Male Study is urban Danish male workers, aged 40–59 years in 1970–1971. It is unknown whether the findings of this study are relevant also for females, younger workers, self-employed individuals or workers from other (eg, rural) communities and nationalities. Workers with pre-existing cardiovascular diseases were excluded from this study. However, a positive but statistically non-significant association was found between physical demands at work and all-cause mortality, and a high physical fitness was associated with a substantially reduced risk for IHD and all-cause mortality (22)

Concluding remarks

Men with low and medium levels of physical fitness have an increased risk of cardiovascular and all-cause mortality if exposed to high physical work demands. Due to the relatively small size of the population who could be classified as being highly fit in this study, further investigation of the risk for mortality from high physical work demands in larger populations with high physical fitness is recommended. Our observations suggest that – among men with high physical work demands – being physically fit protects against adverse cardiovascular effects.

References

1. Krause N, Brand RJ, Kaplan GA, Kauhanen J, Malla S, Tuomainen T-P, et al. Occupational physical activity, energy expenditure and 11-year progression of carotid atherosclerosis. Scand J Work Environ Health. 2007;33(6):405–24.

2. Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. The interplay between physical activity at work and during leisure time – risk of ischemic heart disease and all-cause mortality in middle-aged Caucasian men. Scand J Work Environ Health. 2009;35(6):466–74.

3. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA. 2005;293(3):293–4.

4. Leitzmann MF, Park Y, Blair A, Ballard-Barbash R, Mouw T, Hollenbeck AR, et al. Physical activity recommendations and decreased risk of mortality. Arch Intern Med. 2007;167(22):2453–60.

5. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc. 2007;39(8):1423–34.

6. Åstrand P-O, Rodahl K. Textbook of work physiology. Physiological bases of exercise. New York (NY): McGraw-Hill Book Company; 1986.

7. Blair SN, Kampert JB, Kohl HW, Barlow CE, Macera CA, Paffenbarger RS, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA. 1996;276(3):205–10.

8. Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW. Physical-fitness and all-cause mortality – a prospective-study of healthy-men and women. JAMA. 1989;262(17):2395–401.

9. Erikssen G, Liestøl K, Bjørnholt J, Thaulow E, Sandvik L, Erikssen J. Changes in physical fitness and changes in mortality. Lancet. 1998;352(9130):759–62.

10. Hein HO, Suadicani P, Gyntelberg F. Physical-fitness or physical activity as a predictor of ischemic heart disease?: a 17-year follow-up in the Copenhagen Male Study. J Intern Med. 1992;232(6):471–9.

11. Aminoff T, Smolander J, Korhonen O, Louhevaara V. Prediction of acceptable physical work loads based on responses to prolonged arm and leg exercise. Ergonomics. 1998;41(1):109–20.

12. Virkkunen H, Härmä M, Kauppinen T, Tenkanen L. Shift work, occupational noise and physical workload with ensuing development of blood pressure and their joint effect on the risk of coronary heart disease. Scand J Work Environ Health. 2007;33(6):425–34.

13. Gyntelberg F. Physical fitness and coronary heart-disease male residents in copenhagen aged 40-59. Dan Med Bull. 1973;20(1):1–4.

14. Gyntelberg F. One-year and 2-years incidence of myocardial-infarction in copenhagen males aged 40-59. Dan Med Bull. 1975;22(2):81–4.

15. Hein HO, Suadicani P, Gyntelberg F. Ischaemic heart disease incidence by social class and form of smoking: the Copenhagen Male Study – 17 years' follow-up. J Intern Med. 1992;231(5):477–83.

16. Svalastoga K. Prestige, class and mobility. Copenhagen: Munksgaard; 1959.

17. Hansen EJ. Social groups in Denmark. Copenhagen: The Danish National Centre for Social Research; 1984.

18. Brody S, Lardy HA. Bioenergetics and growth. J Phys Chem. 1946;50(2):168–9.

19. Ilmarinen J, Vouhevaara V, Korhonen O, Nygård CH, Hakola T, Suvanto S. Changes in maximal cardiorespiratory capacity among aging municipal employees. Scand J Work Environ Health. 1991;17 suppl 1:99–109.

20. Karlqvist LK, Harenstam A, Leijon O, Scheele P. Excessive physical demands in modern worklife and characteristics of work and living conditions of persons at risk. Scand J Work Environ Health. 2003;29(5):363–77.

21. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. Res Q Exerc Sport. 2000;71(2):S1–S14

22. Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Fitness, work, and leisure-time physical activity and ischaemic heart disease and all-cause mortality among men with pre-existing cardiovascular disease. Scand J Work Environ Health. 2010;36(5):366–372.

Received for publication: 5 November 2009

論文名	Physical demands at work, physical fitness, and 30-year ischaemic heart disease and all-cause mortality in the Copenhagen Male Study
著 者	Holtermann A, Mortensen OS, Burr H, Sogaard K, Gyntelberg F, Suadicani P
雑誌名	Scand J Work Environ Health
巻・号・頁	36(5)　357-365
発行年	2010
PubMedリンク	http://www.ncbi.nlm.nih.gov/pubmed/20352174

対象の内訳

	ヒト	動物	地 域	欧米	研究の種類	縦断研究
対象	一般健常者	空白		(　)		コホート研究
性別	男性	(　)		(　)		(　)
年齢	40-59歳			(　)		前向き研究
対象数	5000～10000			(　)		(　)

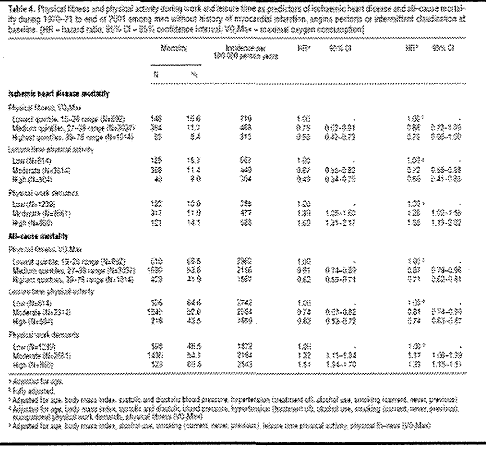
調査の方法

実測	質問紙

アウトカム

予 防	心疾患予防	な し	な し	な し	死亡	(　)
維持・改善	な し	な し	な し	な し	(　)	(　)

図 表



図表掲載箇所: P363, Table4

概 要（800字まで）

本研究は、Copenhagen Male Studyに参加している4,943名の男性を対象に、30年間の追跡調査を行い、体力や肉体労働の度合いと総死亡、虚血性心疾患との関連を検討したものである。最大下自転車エルゴメータテスト（Astrandのノモグラム）により体力を測定した。また質問紙により、余暇時間身体活動、就業中の肉体労働の度合いをスコア化した。体力をVO2Maxの値から15-26、27-38、39-78の3群にに分類している。虚血性心疾患死亡リスクに関して、体力の一番低いグループと比較すると、中間のグループで0.88(95%信頼区間:0.72-1.09)、高いグループで0.75(0.56-1.00)とリスクの減少傾向がみられた。総死亡に関しては、体力の一番低いグループと比較すると、中間のグループで0.87(0.79-0.96)、高いグループで0.71(0.62-0.81)とこちらは有意なリスク減少が明らかとなった。また、多くの肉体労働を要する職業に就いている男性のうち、体力が低いまたは中間のグループに属する者は、虚血性心疾患死亡、総死亡共に有意なリスク増加がみられた。

結 論（200字まで）

中年男性コホート集団（白人）において、有酸素能力の高い男性は有酸素能力の低い男性と比較して、総死亡リスクが有意に減少することが明らかとなった。虚血性心疾患死亡においては、有意ではないもののリスクの減少傾向が認められた。また、多くの肉体労働を要する職業に就いている男性は、有酸素能力を高めることで虚血性心疾患死亡、総死亡共にリスクを減少させることが明らかと

エキスパートによるコメント（200字まで）

身体活動基準の策定に用いられた研究の1つである。約5000名の集団を約30年間の追跡調査により、体力と身体活動量との相互作用を検討した研究である。体力を高くすることにより、職業上、多くの肉体労働を要する人でも死亡のリスクを軽減できることを示した重要な研究である。

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